Induced pluripotency and oncogenic transformation are related processes.

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Public Summary:
Induced pluripotent stem cells (iPSC) have the potential for creating patient-specific regenerative medicine therapies, but the links between pluripotency and tumorigenicity raise important safety concerns. More specifically, the methods employed for the production of induced pluripotent stem cells (iPSC) and oncogenic foci (OF), a form of in vitro produced tumor cells, are surprisingly similar, raising potential concerns about iPSC. To test the hypotheses that iPSC and OF are related cell types and, more broadly, that the induction of pluripotency and tumorigenicity are related processes, we produced iPSC and OF in parallel from common parental fibroblasts. When we compared the transcriptomes of these iPSC and OF to their parental fibroblasts, similar transcriptional changes were observed in both iPSC and OF. A significant number of genes repressed during iPSC formation were also repressed in OF, including a large cohort of differentiation-associated genes. iPSC and OF shared a limited number of genes that were upregulated relative to parental fibroblasts but gene ontology analysis pointed toward monosaccharide metabolism as upregulated in both iPSC and OF. iPSC and OF were distinct in that only iPSCs activated a host of pluripotency-related genes, while OF activated cellular damage and specific metabolic pathways. We reprogrammed OF to produce iPSC-like cells, a process dependent on Nanog. However, the reprogrammed OF (ROF) had reduced differentiation potential compared to iPSC, suggesting that oncogenic transformation leads to cellular changes that impair complete reprogramming. Taken together, these findings support a model in which OF and iPSC are related, yet distinct cell types, and in which induced pluripotency and induced tumorigenesis are similar processes.

Scientific Abstract:
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